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PROCEDURES FOR DEVELOPING SCREENING LEVELS

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INTRODUCTION AND PURPOSE

These procedures summarize the process used by staff of the Air Quality Division's (AQD's) Toxics Unit to develop screening levels for the implementation of Michigan's air toxic rules (Rules 224 - 232). The air toxic rules apply to any new or modified process for which an application for a permit to install is required, and which emits a toxic air contaminant. There are two basic requirements of the air toxic rules. First, each source must apply the best available control technology for toxics (T-BACT) (Rule 224). After the application of T-BACT, the maximum ambient concentration of each toxic air contaminant cannot exceed its screening level (Rule 225 - 232).

The original version of these procedures, dated July 6, 1995, were prepared at the request of the Air Advisory Group to provide a better understanding of the process used by staff of the Toxics Unit to develop screening levels. This version has been updated to reflect changes to the air toxics rules that became effective in November 1998, as well as any other changes in procedures that have occurred since 1995.

Several acronyms will be used in these procedures. The first time the acronym is used, it will be defined. Appendix C contains a list of acronyms used in this document, along with the respective definition.

CONTACTS

For additional information or questions regarding these procedures, call 517-335-6989, and request to speak to a toxicologist in the Toxics Unit.

PRIORITY

The Toxics Unit generally develops screening levels for toxic air contaminants after receiving a request from the AQD's Permit Section. Requests to develop screening levels are processed based upon the date they are received from the Permit Section, unless a priority is requested by one of the supervisors in the Permit Section. After a request for a screening level is received from the Permit Section, it is logged in and assigned to one of the toxicologists. Priority for screening levels requested or needed outside the permitting process are established on a case-by-case basis, taking into consideration the specific factors and needs.

LITERATURE REVIEW

Upon receiving a request for a screening level, the toxicologist initiates a search of relevant databases,

references, and the scientific literature. The extent of this search depends upon the information obtained from key references or databases, the toxicity of the compound, and the predicted ambient impact (PAI). For example, if the U.S. Environmental Protection Agency (EPA) has established a reference concentration (RfC) for a chemical that is published in EPA's Integrated Risk Information System (IRIS), and there is no indication that the chemical is carcinogenic, then the initial threshold screening level (ITSL) is determined from the RfC, and no further evaluation is done. The process for conducting searches of the literature is discussed further in the section on Guidelines for Conducting a Search of the Literature.

DEVELOPMENT OF THE SCREENING LEVEL

The development of screening levels requires the judgment of highly trained toxicologists to evaluate and interpret scientific studies dealing with the toxic effects from exposure to various chemical substances. In evaluating the quality of the study, the toxicologists consider many things such as purity of substance tested, physical form of the substance, vehicle used for administration of dose, volume of material administered, housing and feeding conditions of animals, the number of dose groups, spacing of dose groups, number of animals per dose group, dose levels, exposure duration, duration of study, observation periods, effects evaluated and reported, and statistical analyses performed.

Guidelines have been developed by the EPA that outline toxicological testing protocols that are acceptable for testing requirements under the Toxic Substance Control Act (TSCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Likewise, the Organization for Economic Co-operation and Development (OECD) has developed guidelines that provide a framework for each toxicity test which is sufficiently well defined to enable it to be carried out in a similar manner in different countries and to produce results that will be fully acceptable to various regulatory bodies. More recently, the EPA has developed "harmonized guidelines." The EPA has developed these guidelines through a process of harmonization that blended testing guidance and requirements for TSCA, FIFRA, and OECD. The purpose for harmonizing these guidelines into a single set is to minimize variations among the testing procedures that must be performed to meet the requirements of TSCA and FIFRA. The harmonized guidelines may be accessed through the Internet at http://www.epa.gov/docs/OPPTS_Harmonized/abguide.txt.html. Toxicity tests meeting these guidelines would generally be considered good quality tests; however, often much of the available data falls short of these guidelines, especially for studies done prior to the establishment of these guidelines. In these cases, the toxicologist must use professional judgment in evaluating the quality of an individual study and interpreting the significance of the overall database.

A. Chemicals with a PAI less than $0.1 \mu\text{g}/\text{m}^3$ (micrograms per cubic meter)

If the chemical has a PAI less than $0.1 \mu\text{g}/\text{m}^3$, a quick screen of select databases or references is done to determine if data are available to indicate the chemical should be considered a carcinogen according to Rule 103(c), or if it is highly toxic such that the screening level may be less than $0.1 \mu\text{g}/\text{m}^3$. Examples of chemicals that would warrant further review because they may be considered highly toxic include those with a 4-hour inhalation lethal concentration 50 (LC50) less than $2 \text{ mg}/\text{m}^3$ (milligrams per cubic meter), or an oral rat low dose 50 (LD50) in the range of $10 \text{ mg}/\text{kg}$ (milligrams per kilogram) or less, or repeated dose studies in rats where adverse effects are observed at doses in the range of $1 \text{ mg}/\text{kg}/\text{day}$ or less. Generally, the databases or references checked include IRIS, the Registry of Toxic Effects of Chemical Substances (RTECS), the International Agency for Research on Cancer (IARC) Monographs, and the National Toxicology Program (NTP) Management Status Reports. (See Appendix B for a description of these references.) If no data is available to indicate the chemical is a carcinogen, or the ITSL would be less than $0.1 \mu\text{g}/\text{m}^3$, the PAI is approved, however, no screening level is established for this chemical. If data are available to indicate the chemical may be a carcinogen, or have an ITSL less than $0.1 \mu\text{g}/\text{m}^3$, then further review is done to either establish a screening level or verify that the PAI is acceptable.

B. Chemicals with a PAI greater than $0.1 \mu\text{g}/\text{m}^3$

If the PAI is greater than $0.1 \mu\text{g}/\text{m}^3$, the toxicologist establishes a screening level for the chemical following the methodologies and hierarchy established in Rules 230

232. Occasionally, the toxicologist may approve a PAI greater than $0.1 \mu\text{g}/\text{m}^3$ for some compounds considered to have relatively low toxicity, without determining a screening level. This is only done in those cases where, in the toxicologist's professional judgment, the PAI is significantly lower than the expected screening level. Examples of PAIs approved without determining a screening level include the following: potassium chloride, sodium chloride, and magnesium sulfate at $2.3 \mu\text{g}/\text{m}^3$, potassium carbonate at $0.2 \mu\text{g}/\text{m}^3$, lauryl methacrylate at $5.7 \mu\text{g}/\text{m}^3$, and light aliphatic solvent naphtha at $2.0 \mu\text{g}/\text{m}^3$.

Initial Risk Screening Level (IRSL) and Secondary Risk Screening Level (SRSL)

If the chemical is considered a "carcinogen" based upon the definition in Rule 103(c), then the toxicologist determines the IRSL and the SRSL, using the methodology specified in Rule 229. The EPA Guidelines for Carcinogenic Risk Assessment are also used when appropriate as specified in Rule 229(1)(b) and (c).

In establishing IRSLs and SRSLs, priority is first given to using EPA established inhalation cancer potency values. If EPA has established an inhalation cancer potency value for a chemical that is published in IRIS, that value is used to establish the IRSL and SRSL. If there is no inhalation cancer potency value in IRIS, but there is one listed in EPA's Health Effects Assessment Summary Tables (HEAST), then that value may be used to establish the screening level. If EPA has not established an inhalation cancer potency value, and there is adequate inhalation toxicity data available, the toxicologist establishes the IRSL and SRSL using this data and the procedures identified in Rule 229.

If no inhalation cancer potency value is available from EPA, or can be determined from the data, the toxicologist evaluates the information available from the oral route of exposure. If EPA has established an oral potency value in IRIS (first choice) or HEAST, and data are not available to indicate that oral route to inhalation route extrapolation is inappropriate, this value is used to establish the IRSL and SRSL. If EPA has not established an oral potency value, the toxicologist establishes the IRSL and SRSL following the procedures identified in Rule 229.

Initial Threshold Screening Level

The hierarchy of methods for establishing the ITSL for a chemical is specified in Rule 232. The process used to implement this rule is as follows:

1 If EPA has established an RfC for a chemical, the RfC is used to determine the ITSL. RfCs from IRIS are used as the first choice for establishing an ITSL. If no RfC is available from IRIS, then one from HEAST may be used to establish the ITSL. If no EPA established RfC is available, but toxicity data are available to determine the RfC, the toxicologist determines the RfC using EPA RfC methodology (EPA, 1994), and uses this value to establish the ITSL.

2 If an RfC is not available or cannot be determined from the data, and EPA has established an oral reference dose (RfD), and data are not available to indicate it is inappropriate to extrapolate from the oral route of exposure to exposure via inhalation, then the RfD is used to establish the ITSL. RfDs from IRIS are used as the first choice for establishing the ITSL. If no RfD is available from IRIS, an RfD from HEAST may be used to establish the ITSL. If no EPA established RfD is available, but toxicity data are available to determine the RfD, the toxicologist determines the RfD and uses this value to establish the ITSL.

3 If an RfC or RfD is not available, or cannot be determined from the available data, the occupational exposure level (OEL) is then used to establish the ITSL.

4 If an RfC or RfD is not available, or cannot be determined from the available data, and an OEL

is not available, the toxicological data is evaluated and the methodology in Rules 232(d) - 232(h) is used to establish the ITSL.

5 If no data is available to determine the ITSL, the ITSL is set at the default value of $0.1 \mu\text{g}/\text{m}^3$. Prior to setting the ITSL at the default value, the toxicologist pursues all potential leads for data that could be useful for setting a screening level.

Rule 229(b) provides for use of an alternative methodology to that of Rule 232 for determining the ITSL, provided it is determined to be more appropriate, based on toxicological grounds and supported by the scientific data.

LIST OF SCREENING LEVELS

The Toxics Unit maintains a list of all screening levels that have been established to date. Once a year a complete list of all screening levels established to date is published. Every two months, the Toxics Unit prepares a list of screening levels that have been revised or newly established since the last complete list was published. It should be noted, however, that in general, no revisions of screening levels are being done at this time, unless significant new data is brought to the attention of the Toxics Unit, or the EPA updates an RfC, RfD, or cancer potency value. EPA updates IRIS randomly; staff of the Toxics Unit checks the website (www.epa.gov/iris) for new or revised RfCs, RfDs, and cancer potency values. Screening levels are then revised or added to the list as appropriate.

The lists of screening levels are available electronically on our website at: www.michigan.gov/deg under "Air," then "Air Toxics." The Toxics Unit also maintains an electronic mailing list ([Environmental Listserver Subscriptions](#)) for people who wish to subscribe to receive electronic updated lists as they become available. For those wishing to receive a hard copy of the most recently updated list or to add your name to the regular mailing list, contact Sheila Blais at 517-335-6989, by fax at 517-335-3122 or by e-mail at blaiss@michigan.gov.

GUIDELINES FOR CONDUCTING A SEARCH OF THE LITERATURE

When a request is received by the Toxics Unit for the development of a screening level, a search of the literature is initiated by the toxicologist. This search includes the review and evaluation of various databases, books, documents, and the scientific literature. The standard references checked for the search of the literature are listed on the Reference Check List (Appendix A). A reference check list is initiated for each chemical to track which references have been checked, and the date the check was completed. A short description of each reference found on the Reference Check List is given in Appendix B.

The purpose of the literature search is to identify the available toxicological data for the chemical, and then to use this data in determining the appropriate screening level. As outlined below, the extent of this search depends upon the information obtained from key references, the toxicity of the compound, and the PAI.

Literature Search for Chemicals with a PAI less than $0.1 \mu\text{g}/\text{m}^3$

If the chemical has a PAI less than $0.1 \mu\text{g}/\text{m}^3$, a quick screen of select databases or references is done to determine if data are available to indicate the chemical should be considered a carcinogen according to Rule 103(c), or if it is highly toxic such that the screening level may be less than $0.1 \mu\text{g}/\text{m}^3$. Examples of chemicals that would warrant further review because they may be considered highly toxic include those with a 4-hour inhalation LC50 less than $2 \text{mg}/\text{m}^3$, or an oral rat LD50 in the range of $10 \text{mg}/\text{kg}$ or less, or repeated dose studies in rats where adverse effects are observed at doses in the range of $1 \text{mg}/\text{kg}/\text{day}$ or less. Generally, the databases or references checked include: IRIS, RTECS, IARC Monographs, and NTP Management Status Reports. (See Appendix B for a description of these

references.) If no data are available to indicate the chemical is a carcinogen, or the ITSL would be less than $0.1 \mu\text{g}/\text{m}^3$, the PAI is approved, however, no screening level is established for this chemical. If data are available to indicate the chemical may be a carcinogen or have an ITSL less than $0.1 \mu\text{g}/\text{m}^3$, then further review is done to either establish a screening level or verify that the PAI is acceptable.

Literature Search for Chemicals with a PAI greater than $0.1 \mu\text{g}/\text{m}^3$

If the chemical has a PAI greater than $0.1 \mu\text{g}/\text{m}^3$ and a screening level will be established, a full search of the literature is initiated, which generally includes reviewing all references found on the Reference Check List. Exceptions to this include the following:

1 If an EPA derived RfC is available, no other references are checked, except the quick screen for carcinogenicity data summarized above in the section on literature searches for chemicals with a PAI less than $0.1 \mu\text{g}/\text{m}^3$.

2 If an EPA derived inhalation cancer potency value is available, no other references are checked.

When doing a full search of the literature, the toxicologist utilizes summaries or evaluations of the scientific literature done by other groups to help expedite the review process. The following guidelines are used in these cases:

1 Check the Environmental Protection Based Chemical Criteria Database (EPBCCD) to determine if the chemical has already been evaluated by another division in the Michigan Department of Environmental Quality (MDEQ). Review any existing evaluations to determine if further evaluation is necessary.

2 Comprehensive review documents published by the EPA, Agency for Toxic Substances and Disease Registry (ATSDR), National Institute of Occupational Safety and Health (NIOSH), or other groups may be used to limit the extent of the Chemical Abstract Services (CAS) on-line or National Library of Medicine (NLM) searches, or to limit the review of original articles. Examples of documents that may be useful in this regard are EPA's Health Assessment Documents, ATSDR's Toxicological Profiles, and NIOSH's Criteria for a Recommended Standard documents. If a review document is used to limit the on-line database searches, the CAS on-line and NLM searches should cover the period of time from at least one year before the most recent comprehensive review document was published, to the present.

APPENDIX A: REFERENCE CHECK LIST

Chemical Name: _____ CAS No.: _____

Assigned to: _____ Date logged in Masterlog: _____

REFERENCE RESULT/NAME DATE

AQD Chemical Files (23-6) _____ EPBCCD

(J:\TOXICS\EPBCCD\epbccd.mdb) _____ IRIS

(<http://www.epa.gov/iris/search.htm>) _____ HEAST** (**if nothing in**

IRIS) (RA1216.E6H3 year) _____ NIOSH REL

(X:\CCINFO\CCFINDW.EXE) _____ RTECs* (X:\CCINFO\CCFINDW.EXE)

(end shows TLV) _____ ACGIH TLV* (yr _____ TLV/BEI Booklet)

(baseline: RA1229.D6.1991vol.1-3) EPB Access Library (J:\TOXICS\SWQLIB2\Swqlib2.mdb)

_____ NTP Study Database (<http://ntp-server.niehs.nih.gov/>)

_____ CHEMFINDER (<http://chemfinder.cambridgesoft.com/>)

_____ IARC Monographs (www.iarc.fr) _____

Acute Database (N:\Acute Database\Acute database.mdb) _____ (no dashes or spaces)

CAS ONLINE _____

NLM/TOXLINE _____ (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?toxadv>)

IF OTHER SECONDARY REFERENCES AND/OR REVIEWS ARE NECESSARY, CHECK:

KIRK-OTHMER (chemical encyclopedia) _____ (TD196.073V47 c.3)

Patty's Industrial Hygiene & Toxicology _____
(RC967.P371993vol#__ pt#__)

Hazardous Substances Data Bank (HSDB) _____
(<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>)

FINAL FOLLOWUP:

EPBCCD entries done _____ Memos to Chemical File done

_____ Update Masterlog with dates/info

COMMENTS AND/OR OTHER REFERENCES:

*If an ITSL can be determined from an RfC, RfD, or OEL; and data indicates potential carcinogenic effects, do a full review of literature

**If no RfC or inhalation quantitative risk value in IRIS

APPENDIX B: DESCRIPTION OF REFERENCES

AQD Chemical Files - A file is maintained by the Toxics Unit for each chemical for which a screening level is established, and includes information such as the following: memos and correspondence dealing with the basis of the screening level, reference check lists, printouts from IRIS, CAS On-line and NLM/Toxline searches, and other relevant information.

EPBCCD - This database is maintained and used by toxicologists in the MDEQ's AQD, Environmental Response Division (ERD), Surface Water Quality Division (SWQD), and Waste Management Division (WMD). The database contains human health, wildlife, and aesthetic criteria established by the toxicologists in these divisions for use in the various environmental regulatory programs. Included in this database are the screening levels established by staff of the AQD.

IRIS - This electronic database (www.epa.gov/iris) is maintained by the EPA, and contains health risk information that has received EPA-wide consensus. IRIS contains summary information on several hundred chemicals, including such things as RfCs, RfDs, carcinogen risk assessments, and other regulatory information. EPA has made IRIS available to the public.

HEAST - This reference is prepared by EPA's Office of Health and Environmental Assessment. HEAST contains primarily provisional risk assessment information relative to oral and inhalation routes of exposure for chemicals of interest to Superfund, the Resource Conservation and Recovery Act (RCRA), and the EPA in general. The entries in HEAST are limited to chemicals that have undergone review and have the concurrence of individual EPA Program Offices, although the risk assessment information has not had enough review to be recognized as high quality EPA-wide consensus information.

NIOSH Recommended Exposure Levels (REL) - NIOSH is a federal agency responsible for recommending criteria for preventing disease and hazardous conditions in the workplace. RELs are examples of such criteria. RELs are occupational exposure limits recommended by NIOSH as being protective of worker health and safety over a working lifetime. RELs are listed in the NIOSH Pocket Guide to Chemical Hazards.

RTECS - This database is prepared and maintained by NIOSH, and contains summary toxicological information on a large number of chemicals. The data is extracted from the scientific literature, however, no evaluation of the data is done by the Registry. All data listed in the Registry are referenced to the sources in which the data appeared. As of June 1992, there were data on more than 111,000 chemicals in the Registry. RTECS is updated regularly, and is available on microfiche from NIOSH, on-line via NLM, and on compact disk from various sources.

American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV) - The ACGIH is a non-governmental organization that develops TLVs as guidelines to assist in the control of health hazards in an occupational setting. These values are listed in a booklet published by the ACGIH each year. The basis for the TLVs is found in ACGIH's Documentation for Threshold Limit Values and Biological Exposure Indices.

Environmental Protection Based (EPB) Access Library - The AQD, SWQD, WMD, and ERD maintain a joint on-line catalogue of reference materials maintained in each division's library. Materials included in the on-line catalogue are primarily those dealing with the toxicological effects of chemicals, and include books, journal articles obtained from the scientific literature, documents from various international, federal and state agencies, and other relevant information. The catalogue may be searched by many different parameters, including chemical name, CAS number, title, author, and key words.

NTP Management Status Report - These reports are available online at <http://ntp->

server.niehs.nih.gov/. They are prepared quarterly by the NTP and provide status information for all toxicological studies conducted by NTP, including carcinogenicity bioassays.

CHEMFINDER – (<http://chemfinder.cambridgesoft.com/>) This website is a chemical search engine that provides synonyms, physical property data, chemical structure, health data, MSDS, regulatory information and other chemical specific data.

IARC Monographs - This series of monographs entitled, IARC Monographs on the Evaluation of Carcinogenic Risk to Humans provides critical reviews and evaluations of the data regarding the carcinogenicity of a large number of chemical, physical, and biological agents. Reviews and evaluations are done by a working group of experts selected by IARC staff in consultation with other experts. This is an ongoing project, and new monographs are published every year and are also available online at www.iarc.fr/.

Acute Database – (n:\acute database\acute database.mdb) This database, compiled by Toxics Unit staff, contains acute toxicity values. The values include only inhalation exposure and were developed by a number of organizations. It is important to note that separate groups created the values for different purposes. There are other acute inhalation values available from other organizations; they have not been included in the database as these values were not readily available for incorporation during the development phase. Values in this database are not used directly in screening level derivation, however they can be used for comparison purposes to determine the amount of variability between acute and chronic numbers or to obtain more toxicity references.

CAS Online - The CAS file is a bibliographic database covering worldwide literature from all areas of chemistry, biochemistry, and chemical engineering from 1967 to the present. The records contain bibliographic information and abstracts which are concise summaries of the major findings reported in the scientific literature. Sources for CA include more than 8,000 journals, patents, technical reports, books, conference proceedings, and dissertations from around the world. About 14,000 records are added every week, with much of the information added to the database on a daily basis. There are over 20 million chemicals in the CAS Registry.

NLM – (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?toxadv>) Primarily the TOXLINE file is searched. The TOXLINE file contains toxicological, pharmacological, biochemical, and physiological effects of drugs and other chemicals. Journals, monographs, technical reports, theses, letters, and meeting abstracts are monitored as well as papers and reports. The TOXLINE file is used to search for existing data (it is no longer updated monthly). Other databases are also searched, e.g. MEDLINE (Note: MEDLINE contains new toxicity references and covers the fields of medicine, nursing, dentistry, veterinary medicine, and the pre clinical sciences from over 3600 international biomedical journals from 1966 to the present); TOXLINE65 and TOXLIT65 (for older citations); and HSDB.

KIRK-OTHMER (Chemical Encyclopedia) -This 27 volume encyclopedia provides a comprehensive description of applied chemistry and chemical engineering, including industrial technology, methods and materials, and the latest scientific advances in chemistry.

Patty's Industrial Hygiene & Toxicology -Patty's is a seven volume compendium of industrial toxicology. It presents information on chemicals that pose a potential threat to the health and safety of workers.

HSDB – (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>) is a toxicology data file on the NLM's Toxicology Data Network (TOXNET®). It focuses on the toxicology of potentially hazardous chemicals. It is enhanced with information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, and related areas.

APPENDIX C: LIST OF ACRONYMS

ACGIH	American Conference of Governmental Industrial Hygienists
AQD	Air Quality Division
ATSDR	Agency for Toxic Substances and Disease Registry
CAS	Chemical Abstract Services
EPB	Environmental Protection Based
EPBCCD	Environmental Protection Based Chemical Criteria Database
EPA	U.S. Environmental Protection Agency
ERD	Environmental Response Division
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
HSDB	Hazardous Substances Data Bank
HEAST	Health Effects Assessment Summary Table
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
IRSL	Initial Risk Screening Level
ITSL	Initial Threshold Screening Level
LC50	Lethal Concentration 50; concentration lethal to 50% of the animals
LD50	Lethal Dose 50; dose lethal to 50% of the animals
MDEQ	Michigan Department of Environmental Quality
mg/kg	Milligrams per kilogram
mg/m ³	Milligrams per cubic meter
NIOSH	National Institute of Occupational Safety and Health
NLM	National Library of Medicine
NTP	National Toxicology Program
OECD	Organization for Economic Co-operation and Development
OEL	Occupational Exposure Level
PAI	Predicted Ambient Impact
RCRA	Resource Conservation and Recovery Act
REL	Recommended Exposure Level
RfC	Reference Concentration
RfD	Reference Dose
RTECS	Registry of Toxic Effects of Chemical Substances
SRSL	Secondary Risk Screening Level
SWQD	Surface Water Quality Division
T-BACT	Best Available Control Technology for Toxics
TLV	Threshold Limit Value
TSCA	Toxic Substances Control Act
µg/m ³	Micrograms per cubic meter
WMD	Waste Management Division